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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION under 37 CFR 1.53(b)(2).

INVENTOR(S)

LAST NAME	FIRST NAME	MIDDLE INITIAL	RESIDENCE (CITY AND EITHER STATE OR FOREIGN COUNTRY)
Chen	Jeff	Z.	London, Canada
Battista	Jerry	J.	London, Canada
Goldman	Samuel	P.	London, Canada

☐ *Additional inventors are being named on the __0___ separately numbered sheets attached hereto*

TITLE OF THE INVENTION (280 characters max)

Fast Inverse Dose Optimization (FIDO) for IMRT via Matrix Inversion without Negative Beamlet Intensities

CORRESPONDENCE ADDRESS

Direct all correspondence to:

☐ Customer Number [ ] *Place Customer Number Bar Code Label here*

OR *Type Customer Number Here*

☒ Firm *or* Individual Name	The University of Western Ontario Attention: Theresa Russelo, Technology Transfer Coordinator				
Address	Industry Liaison				
Address	Stevenson-Lawson Building, Rm. 328				
City	London	State	Ontario	ZIP	N6A 5B8
Country	Canada	Telephone	519-661-4183	Fax	519-661-3907

ENCLOSED APPLICATION PARTS *(check all that apply)*

☒ Specification *Number of Pages* 13 ☒ Small Entity Statement

☐ Drawings *Number of Sheets* 0 ☐ Other (specify)

METHOD OF PAYMENT FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

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☐ Yes, the name of the U.S. Government agency and the Government contract number are:_____

Respectfully submitted,

SIGNATURE _____ Date 08/18/2004

TYPED OR PRINTED NAME Rob Herold, Acting Director, Industry Liaison

TELEPHONE: 519-661-4183

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
10/136,786	04/30/2002	Arthur Katzakian JR.	ECOT-002

CONFIRMATION NO. 9020

33321
DANIEL P. MAGUIRE
423 E ST.
DAVIS, CA 95616

"OC0000000010439212"

Date Mailed: 07/07/2003

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 06/19/2003.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

R. Baltimore

REGINA D TAMPER BALTIMORE
3600 (703) 308-7444

ATTORNEY/APPLICANT COPY

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10/136,786	04/30/2002	Arthur Katzakian JR.	ECOT-002

CONFIRMATION NO. 9020

OC000000010439188

24353
BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD RD
SUITE 200
MENLO PARK, CA 94025

Date Mailed: 07/07/2003

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 06/19/2003.

- The Power of Attorney to you in this application has been revoked by the assignee who has intervened as provided by 37 CFR 3.71. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

R. Baltimore

REGINA D TAMPER BALTIMORE
3600 (703) 308-7444

NEW ATTORNEY/AGENT COPY

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STATEMENT CLAIMING SMALL ENTITY STATUS (37 CFR 1.9 (f) & 1.27 (b)) -- NONPROFIT ORGANIZATION

Docket Number (Optional)

Applicant, Patentee, or Identifier: The University of Western Ontario

Application or Patent No.: _____

Filed or Issued: _____

Title: Fast Inverse Dose Optimization (FIDO) for IMRT via Matrix Inversion without Negative Beamlet Intensities

I hereby state that I am an official empowered to act on behalf of the nonprofit organization identified below:

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NAME OF PERSON SIGNING Rob Herold

TITLE IN ORGANIZATION OF PERSON SIGNING Acting Director

ADDRESS OF PERSON SIGNING Stevenson-Lawson Building, Room 328, London, Ontario N6A 5B8

SIGNATURE _____ DATE August 18, 2004

Daniel P. Maguire
Attorney at Law
423 E Street
Davis, California 95616
(530) 750-3661
fax: (530) 750-3793

Facsimile Cover Sheet

Date: August 18, 2004 No. of Pages (including cover): 3

To:

Name	*Company*	*Facsimile Number*	*Telephone Number*
Bill Rhodes	Digipat	(703) 413-3668	(703) 413-3667

Re: *Serial No: 10/136,786; File No.: 134.05*

Message:

Dear Mr. Rhodes:

I am sending herewith the "Notice Regarding Change of Power of Attorney" and "Notice of Acceptance of Power of Attorney" which we discussed on the phone today. Please let me know if this is what you need. Thank you for your help with this matter.

Jenny Ramsey
Secretary to Daniel P. Maguire

Fast Inverse Dose Optimization (FIDO) for IMRT via Matrix Inversion without Negative Beamlet Intensities

S. P. Goldman[1], J. Z. Chen[2] and J. J. Battista[2]

[1]Dept. of Physics & Astronomy, University of Western Ontario, London, Ontario, Canada
[2]Dept. of Oncology, University of Western Ontario and London Regional Cancer Centre, London, Ontario Canada

E-mail: goldman@uwo.ca

Abstract

A fast optimization algorithm is very important for inverse planning of Intensity Modulated Radiation Therapy (IMRT), and for adaptive radiotherapy of the future. Conventional numerical search algorithms such as the conjugate gradient search, with positive beam weight constraints, generally require numerous iterations and may produce suboptimal dose results due to trapping in local minima. A direct solution of the inverse problem using conventional quadratic objective functions without positive beam constraints is more efficient but will result in unrealistic negative beam weights. We present here a direct solution of the inverse problem which does not yield unphysical negative beam weights. The objective function for the optimization of a large number of beamlets is reformulated such that the optimization problem is reduced to a linear set of equations. The optimal set of intensities is found through a matrix inversion, and negative beamlet intensities are avoided without the need for externally imposed ad-hoc constraints. The method has been applied to a test phantom and to a few clinical radiotherapy problems. We achieve highly conformal primary dose distributions with very short optimization times. Typical optimization times for a single anatomical slice (2D) using a Matlab matrix inversion routine in a single processor desktop computer, are: 0.03 sec. for 400 beamlets; 0.25 sec. for 1,000 beamlets; 3.5 sec. for 2,000 beamlets and 8 sec for 3,000 beamlets. In conclusion, the new method provides a fast and robust technique to find a global minimum that yields excellent results for the inverse planning of IMRT.

Keywords: Inverse planning, optimization, objective function.

Author for correspondence:
[1]S. P. Goldman
Dept. of Physics & Astronomy
The University of Western Ontario
London, Ontario
CANADA N6A 3K7

1. Introduction

Intensity Modulated Radiation Therapy (IMRT) is becoming a new standard technique for radiotherapy. Given the availability of online imaging tools (Mackie et al 1999, Groh et al 2001, Jaffray et al 2002) and the improved conformal dose distributions obtained through IMRT and its dynamic delivery features, adaptive radiotherapy becomes an important factor to be considered. A fast and reliable optimization algorithm is crucial not only for designing good radiation treatment plans but also for the successful implementation of future interactive adaptive treatment techniques. Conventional optimization algorithms using numerical searches such as the conjugate gradient search (Smith and Lasdon 1992, Spirou and Chui 1998) with positive beam weight constraints usually require numerous iterations (i.e. long computation times) and may result in suboptimal plans due to trapping in local minima of the objective function. A direct solution of the inverse problem using conventional quadratic objective functions without imposing positive beam constraints would be computationally faster but will result in unrealistic negative beam weights. We present here a fast inverse dose optimization (FIDO) method for the direct solution of the inverse problem that avoids negative beamlet weights and preserves efficiency.

The most fundamental requirements of a radiation treatment optimization are: (*i*) dose is homogeneously deposited in the Planning Target Volume (PTV); (*ii*) the dose deposited in any Organ At Risk (OAR) does not exceed a threshold value and ideally should be zero; (*iii*) the dose deposited in the rest of the organs and tissue not included in the PTV and OARs, should be as low as is reasonably achievable (ALARA principle) to minimize the risk of secondary carcinogenesis. We will call these global whole-body regions "all the rest", abbreviated as ATR; (*iv*) the planned dose gradient crossing the PTV boundaries should be as high as possible, but it is subsequently degraded by practical considerations such as patient setups. Optimizations are pursued by the minimization of a positive-definite objective function. A successful optimization will yield a global minimum to this objective function in a short computation time with physically achievable beamlet intensities.

This work reintroduces an approach to radiation treatment optimization that is very fast by solving a linear system of equations and yields a global minimum of the objective function without the use of a search routine. The possibility of such a direct optimization scheme has been known for decades but it has been "impossible" to implement rigorously using conventional quadratic objective functions because optimized results are only achievable with unphysical negative beamlet intensities (Webb 2003). If an ad-hoc condition requiring the beamlet intensities to be positive is introduced (e.g. force negative values to be zero), the linear solution method yields a dose distribution with artefacts and non-uniformities. Alternatively, one may pursue a minimization of the objective function by a direct search over all possible positive beam intensities, but this is a very time-consuming "trail and error" approach. Practically, such approaches become prohibitive if repeat optimizations would be desirable but avoided; the dose results are sometimes deemed "good enough" prematurely.

In this work the negative-intensities problem is considered *within the objective function* and not as an externally imposed ad-hoc requirement. In this way the objective function remains quadratic and the single global minimum is obtained by efficient matrix inversion. Only primary KERMA has been included in the calculations reported here; however an extension to full 3D dose optimization is straightforward.

1.1 Conventional objective function

For simplicity of the formulation we will consider a single PTV, a single OAR and the ATR region. A typical objective function $\tilde{O}$ satisfying the optimization conditions stated above is of the form:

$$\tilde{O} = p_{PTV}O_{PTV} + p_{OAR}\tilde{O}_{OAR} + p_{ATR}\tilde{O}_{ATR} \qquad (1)$$

where the p_k are importance coefficients and the objectivity terms are:

$$O_{PTV} = \sum_{x \in PTV} \left(\sum_{i}^{\text{all beamlets}} w_i d_i(x) - d^{PTV} \right)^2, \tag{2a}$$

$$\tilde{O}_{OAR} = \sum_{x \in OAR} \left(\sum_{i}^{\text{all beamlets}} w_i d_i(x) \right)^2, \tag{2b}$$

and

$$\tilde{O}_{ATR} = \sum_{x \in ATR} \left(\sum_{i}^{\text{all beamlets}} w_i d_i(x) \right)^2, \tag{2c}$$

where w_i is the weight of beamlet i, d_i is the dose deposited at destination point x by beamlet i and d^{PTV} is the dose prescribed to the PTV. For the moment and for the sake of clarity, the importance coefficients in the objective function $\tilde{O}$ (eq. 1) are constants. Later in the paper (Section 3.1) we will generalize this technique to the case of position-dependent importance coefficients (Shou and Xing 2004).

The objective function $\tilde{O}$ (eq. 1) is positive and has an absolute minimum equal to zero when each of the terms is zero. This means a dose equal to d^{PTV} at each point inside the *PTV* and a zero dose elsewhere. The main reason for the traditional appearance of negative weights upon optimization of the objective function $\tilde{O}$ is the fact that we impose two conflicting conditions: we require $\tilde{O}_{OAR} = \tilde{O}_{ATR} = 0$ and yet we require radiation to pass through the ATR (and possibly OARs) to reach the PTV.

1.2 Change in the non-PTV terms of the objective function

A correct requirement on the OAR and ATR terms in the objective function is that they should be *minimized to attain zero only if the weights of all the beamlets passing through these regions are zero.* This requirement is satisfied if we use new objectivity terms of the form

$$O_{ATR} = \sum_{x \in ATR} \sum_{i}^{\text{all beamlets}} w_i^2 d_i^2(x). \tag{3}$$

$$O_{OAR} = \sum_{x \in OAR} \sum_{i}^{\text{all beamlets}} w_i^2 d_i^2(x). \tag{4}$$

The terms (3) and (4) will be zero only if w_i is zero for all i. These terms do not allow the objective function to be zero through "destructive interference" effects between beamlets. Notice that the condition

$$\sum_{x} \sum_{i}^{\text{all beamlets}} w_i^2 d_i^2(x) = 0$$

is necessary and sufficient to satisfy

$$\sum_{x} \left(\sum_{i}^{\text{all beamlets}} w_i d_i(x) \right)^2 = 0 \quad \text{with} \quad w_i \geq 0 \quad \text{for all } i.$$

1.3 A new family of symmetry terms in the objective function

We also introduce a family of symmetry terms to the objective function to improve the conformity (ICRU 1993 and ICRU 1999) of the dose distribution with positive weights for beamlets. The main purpose of these terms is to eliminate the interference effects that lead to

the appearance of negative weights. As a first example that we used for the results presented in this work, the term is of the form

$$O_{sym} = \sum_{i}^{\text{all beamlets}} (w_i - 1)^2 . \tag{5a}$$

This term complements the zero-limit for the beamlet weights in the OAR and ATR terms of the objective function with an equal-weight limit for all beamlets, the usual initial set of weights before optimization (cylindrically symmetric distribution of beams for a beam-source rotating around an isocentre). The term O_{sym} in Eq. (5a) is positive and its minimum is zero - with the weights normalized to

$$\sum_{i}^{\text{all beamlets}} w_i = N = \text{total number of beamlets},$$

the minimum $O_{sym} = 0$ corresponds to a symmetric beamlet arrangement with $w_i = 1$ for all beams.

A slightly different symmetry condition, less restrictive on the beamlet weights is the requirement of a symmetric *beam* (not beamlet) distribution. Calling now $w_j^{(i)}$ the weight of beamlet j inside beam i (i.e. one of the beamlets in the beam incident from the i-th gantry angle, and calling

$$W^{(i)} = \sum_{j}^{\substack{\text{all beamlets} \\ \text{inside beam } i}} w_j^{(i)} .$$

the symmetry condition on the beams becomes

$$O'_{sym} = \sum_{i}^{\text{all beams}} \left(W^{(i)} - 1\right)^2 . \tag{5b}$$

Other possible forms of the symmetry term are

$$O''_{sym} = \sum_{i}^{\text{all beamlets}} w_i^2 , \tag{5c}$$

$$O'''_{sym} = \sum_{x \in \text{all contours}} \sum_{i}^{\text{all beamlets}} w_i^2 d_i^2(x) , \tag{5d}$$

and

$$O^{iv}_{sym} = \sum_{\substack{x \in \text{all contours} \\ \text{except PTV}}} \sum_{i}^{\text{all beamlets}} w_i^2 d_i^2(x) . \tag{5e}$$

The term (5c) is less restrictive than (5a) given that the impossibility of having all the weights equal to zero results in an uneven distribution of *positive* beamlet weights. The net effect of term (5d) is to induce an even distribution of dose deposition *everywhere* regardless of contour, while (5e) will tend to smear the dose distribution everywhere except inside the PTV. Note that, if desired, the contour not included in the expression (5e) can be arbitrarily chosen. The symmetry term included in the objective function for results presented in this work is the even-beamlet term (5a).

1.4 The new objective function

As a result of the above initial considerations, the new objective function is formulated as:

$$O = p_{PTV}O_{PTV} + p_{OAR}O_{OAR} + p_{ATR}O_{ATR} + p_{sym}O_{sym} \tag{7a}$$

or

$$O = p_{PTV}\sum_{x\in PTV}\left(\sum_{i}^{\text{all beamlets}} w_i d_i(x) - d^{PTV}\right)^2 + p_{OAR}\sum_{x\in OAR}\sum_{i}^{\text{all beamlets}} w_i^2 d_i^2(x) + p_{ATR}\sum_{x\in ATR}\sum_{i}^{\text{all beamlets}} w_i^2 d_i^2(x) + p_{sym}\sum_{i}^{\text{all beamlets}}\left(w_i - 1\right)^2 \tag{7b}$$

Notice that a very large value of the importance parameter p_{sym} relative to the other importance parameters will result in an equal-weight beamlet weight distribution regardless of the shape or size of the contours being treated. This is a very strong condition that avoids negative weights but results in a non-optimized treatment plan. In practice, one needs very small relative values of p_{sym} to avoid negative weights. Increasing the value of p_{sym} will result in a "smearing" of the dose distribution eliminating hot spots. Different relative values of p_{ATR} and p_{sym} will result in different dose distributions in the regions outside the OAR and PTV. Thus, this formulation introduces flexibility and algorithmic control, depending on the anatomy layout and clinical objectives.

2. Optimization

2.1 Condition for the minimum of the objective function

With the modifications introduced above, the objective function remains quadratic in the weights and the optimization problem for all the beam intensities is reduced to the solution of a system of linear algebraic equations. Given that the OAR and ATR terms of the objective function are identical in form, for the sake of clarity we will initially omit the ATR term in the derivation below and reintroduce it at the end. With this in mind the objective function becomes

$$O = p_{PTV}\sum_{x\in PTV}\left(\sum_{i}^{\text{all beamlets}} w_i d_i(x) - d^{PTV}\right)^2 + p_{OAR}\sum_{x\in OAR}\sum_{i}^{\text{all beamlets}} w_i^2 d_i^2(x) + p_{sym}\sum_{i}^{\text{all beamlets}}\left(w_i - 1\right)^2 \tag{9}$$

The minimum of O is obtained by requiring

$$0 = \frac{\partial O}{\partial w_j} \quad \text{for all } w_j. \tag{10}$$

Using Eq. (9) this condition results in

$$0 = 2p_{PTV}\sum_{x\in PTV} d_j(x)\left(\sum_{i}^{\text{all beamlets}} w_i d_i(x) - d^{PTV}\right) + 2p_{OAR}\sum_{x\in OAR} w_j d_j^2(x) + 2p_{sym}\left(w_j - 1\right) \tag{11}$$

Exchanging the order of summations we can write (11) as:

$$0 = p_{PTV} \sum_{i}^{\text{all beamlets}} w_i \sum_{x \in PTV} d_i(x) d_j(x) - p_{PTV}\, d^{PTV} \sum_{x \in PTV} d_j(x) + p_{OAR} \sum_{i}^{\text{all beamlets}} w_i \sum_{x \in OAR} d_i(x) d_j(x) \delta_{ij} + p_{sym} \sum_{i}^{\text{all beamlets}} w_i\, \delta_{ij} - p_{sym} \tag{12}$$

where δ_{ij} is a Krönecker delta function:

$$\delta_{ij} = \begin{cases} 1 & \text{if } i = j \\ 0 & \text{otherwise} \end{cases}.$$

We define now the weight-independent arrays

$$\alpha_{ij}^{region_k} = \sum_{x \in region_k} d_i(x) d_j(x) \tag{13}$$

and

$$\beta_j^{region_k} = d^{region_k} \sum_{x \in region_k} d_j(x). \tag{14}$$

where d^{region_k} is the dose required in region k and $\beta_j^{region_k}$ is a one-dimensional array – as we see in expression (13), the element j contains the sum over all points in a region of the dose $d_j(x)$ deposited by beamlet j at each point x in the region. $\alpha_{ij}^{region_k}$ is a two dimensional array – as wee in expression (13), the element ij contains the sum over all points in a region of the *product* of the dose $d_i(x)$ deposited by beamlet i and the dose $d_i(x)$ deposited by beamlet j at each point x in the region in which they overlap (i.e. at each point x in the region in which both $d_i(x)$ and $d_j(x)$ are non-zero).

2.2 Solution using matrix inversion

The condition for the minimum of O can now be written as:

$$\sum_{i}^{\text{all beamlets}} w_i \left(p_{PTV} \alpha_{ij}^{PTV} + p_{OAR} \alpha_{ij}^{OAR} \delta_{ij} + p_{sym} \delta_{ij} \right) = p_{PTV}\, \beta_j^{PTV} + p_{sym}. \tag{15}$$

Notice that in the left side of equation (15) the weights are multiplied by the elements of a constant array. Reintroducing now the ATR terms we define the arrays

$$\alpha_{ij} = p_{PTV} \alpha_{ij}^{PTV} + \left(p_{OAR} \alpha_{ij}^{OAR} + p_{ATR} \alpha_{ij}^{ATR} + p_{sym} \right) \delta_{ij} \tag{16}$$

$$\beta_j = p_{PTV} \beta_j^{PTV} + p_{sym}. \tag{17}$$

The linear system of equations to be solved becomes simply

$$\sum_i w_i \alpha_{ij} = \beta_j \tag{18}$$

where w_i is the (unknown) weight or intensity of beamlet i, β_j is a vector of coefficients that depends on the dose deposited by beam i within the PTV, and α_{ij} is a matrix that describes the product of the doses deposited by the intersecting pairs of beamlets i and j on different organs (each organ with its importance coefficient). The set of optimal beam weights is obtained from Eq. (1) by direct inversion:

$$w_i = \sum_j \alpha_{ij}^{-1} \beta_j \tag{19}$$

In other words, the unique solution to the large system of linear equations (18) is obtained quickly and accurately by inverting the array α_{ij} using standard matrix inversion routines. As shown later in the results section, the optimization by matrix inversion is orders of magnitude faster than using a numerical search algorithm to locate a minimum. Moreover, the minimum is unique and global, so that local minima – a major uncertainty in numerical search techniques – are avoided.

A possible complication is that system (19) may become ill-behaved if two beamlets have very similar dose depositions at the same spatial locations. This will result in a near-linear dependence of terms in the system (18) with divergent values in the matrix α^{-1}. The physical meaning is that two (or more) beamlets are nearly identical and then one or more may become unnecessary. This situation and the elimination of redundant beamlets are easily handled by a Singular Value Decomposition approach to the matrix inversion (Press *et al* 1992).

2.3 Optimization with different importance coefficients

The next step in planning is to choose an appropriate set of importance parameters. This is achieved by manual iterations of relative values of the importance parameters or through a programmed search, for example optimizing curves in DVH histograms. With the aid of FIDO either of these approaches becomes feasible given the high speed of optimization; repeat optimizations are not computationally onerous. In particular the "trial and error" setting of the importance coefficients is achieved almost interactively using this optimization routine.

The fast re-optimization with different sets of importance coefficients is due also to the fact that most of the arrays do not need to be recalculated. The arrays α^{organ_k} and β^{organ_k} do not depend on the importance coefficients or the weights of the beamlets (they are calculated for unit weight beamlets), therefore they need to be calculated only once. After the first optimization, the arrays α^{organ_k} and β^{organ_k} are retrieved from memory and the final equation arrays α and β in equations (16) and (17) are calculated quickly by a linear combination of the stored arrays and the new importance coefficients.

3. Extensions

3.1 Region dependent importance coefficients

In the last section we assumed that the importance coefficients for all points inside each contour are constants, *i.e.* the same for each point inside a contour. Consider now the case in which the importance coefficients can actually vary within the region enclosed by a contour (Corutz et al 2003, Shou and Xing 2004) as might be the case if tumour clonogens can be clearly identified with higher probability by new imaging modalities:

$$p_{region_k} = \hat{p}_{region_k} q_{region_k}(x) \tag{20}$$

where $\hat{p}$ is an overall constant and $q(x)$ is a function of position. In this case, we replace the definitions of equations (13) and (14) by

$$\hat{\alpha}_{ij}^{region_k} = \sum_{x \in region_k} q_{region_k}(x) d_i(x) d_j(x) \tag{21}$$

and

$$\hat{\beta}_j^{region_k} = d^{region_k} \sum_{x \in region_k} q_{region_k}(x) d_j(x) . \tag{22}$$

With these, the matrix formulation of the optimization process now becomes:

$$\hat{\alpha}_{ij} = \hat{p}_{PTV}\hat{\alpha}_{ij}^{PTV} + \left(\hat{p}_{OAR}\hat{\alpha}_{ij}^{OAR} + \hat{p}_{ATR}\alpha_{ij}^{ATR} + p_{sym}\right)\delta_{ij} \tag{23}$$

$$\hat{\beta}_j = \hat{p}_{PTV}\,\hat{\beta}_j^{PTV} + p_{sym}\,. \tag{24}$$

The previous linear system of equations of equation (18) is now replaced by

$$\sum_i w_i\hat{\alpha}_{ij} = \hat{\beta}_j \tag{25}$$

and the optimized solution is obtained from (25) by inversion:

$$w_i = \sum_j \hat{\alpha}_{ij}^{-1}\,\hat{\beta}_j \tag{26}$$

As before, if the functional dependence of the importance coefficients remains unaltered, a search of the best set of importance parameters is reduced to a search of the best set $\hat{p}_{region_k}$ in which case the arrays $\hat{\alpha}_{region_k}$ and β_{region_k} do not need to be recalculated. Notice that the introduction of sub-contours is equivalent to this approach if the importance parameters are constant within a sub-contour.

4. The circularly symmetric case

4.1 Symmetry considerations

This simple case is remarkable because it points to the robustness of FIDO in a case in which the traditional objective function, currently in use, fails to yield correct results.

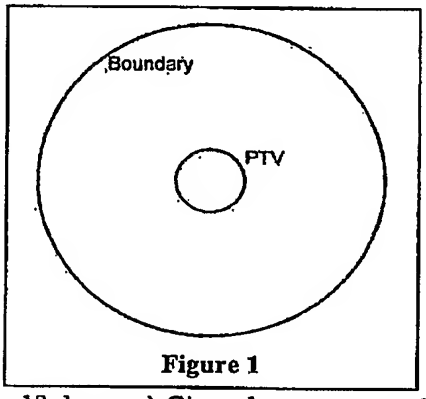

Figure 1

Consider a target region (PTV) with a circular cross section inside a boundary also with a circular cross section as well. Both, the PTV and the exterior boundary, are concentric and are centered at the isocentre as shown in Figure 1 in which the diameters of the PTV and the outside boundary are 8 cm and 40 cm respectively. Consider now an irradiation using arc-therapy with uniform beam intensity (not divided into beamlets), each beam covering exactly the PTV, with a constant gantry angle separation between adjacent beams (*e.g.* for 20 beams the angle separation is 18 degrees.) Given the symmetry of the configuration, the solution should not change if beams are rotated around the centre by an angle that is a multiple of the gantry angle separation between beams. As a consequence of this rotational symmetry, the optimal beam configuration must be such that the weights of all the beams must be identical. If we call w_i the weight of beam i, then $w_i = w_j$ for all the beams or, identically $w_i / w_j = 1$ for all beams, in particular for the beams with the minimum and maximum weights, we should find $w_{min} / w_{max} = 1$.

4.2 Failure of the conventional method

In this case we optimized the conventional objective function

$$O_{conventional} = p_{PTV}O_{PTV} + p_{tissue}\tilde{O}_{tissue}$$

with the *PTV* and *tissue* terms defined respectively in equations (2a) and (2c).

Figures 2 and 3 plot the ratio w_{min} / w_{max} for the configuration shown in Figure 1, as a function of the ratio of the importance parameter for tissue and for PTV. A good optimization

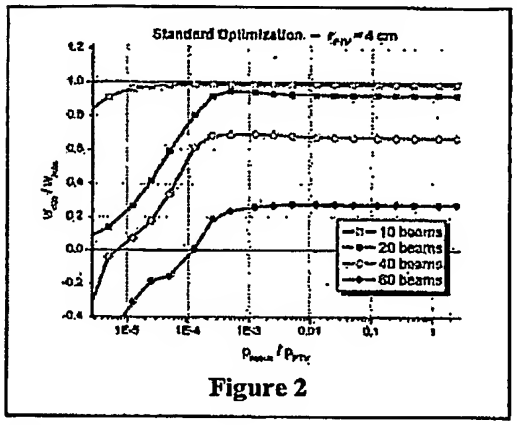

Figure 2

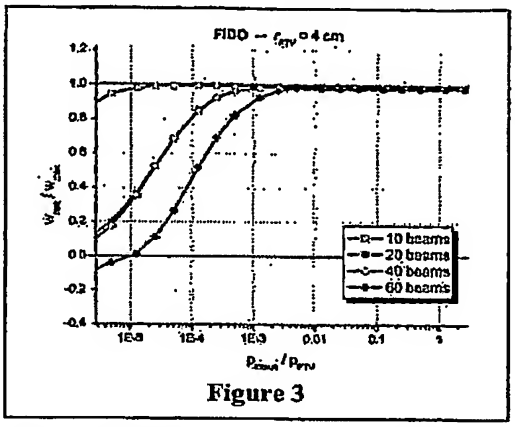

Figure 3

should, as we have seen, yield $w_{min} / w_{max} = 1$. Figure 2 shows the results obtained using the traditional objective function with a numerical search without imposing positive-weights

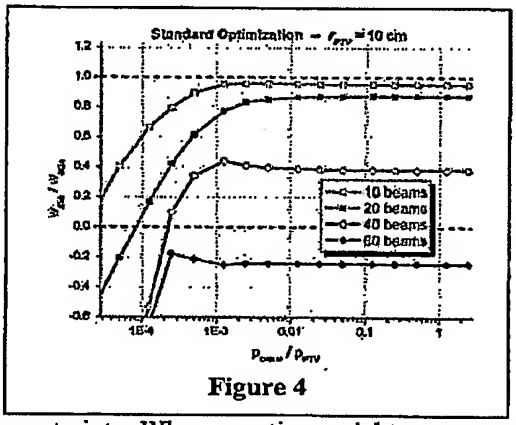

Figure 4

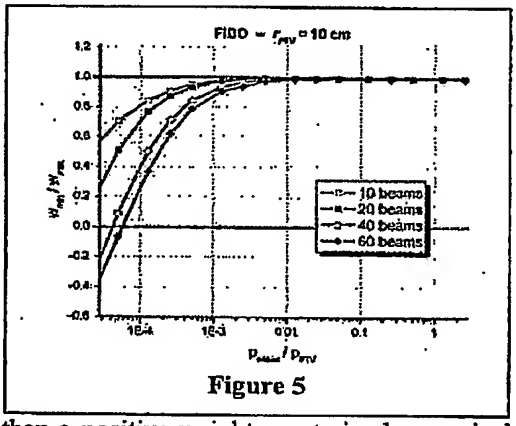

Figure 5

constraints. When negative weights are present then a positive-weight constrained numerical search yields some zero weights for which $w_{min} / w_{max} = 0$. If negative weights are absent, the results using a constrained and an unconstrained numerical search are identical. We see that the traditional optimization yields an incorrect result for any value of p_{tissue}; the results becoming progressively worse as the number of beams is increased. The situation is even worse when a larger PTV diameter is used; as we see in Figure 4 for a PTV with a 20 cm diameter, for 60 beams there is no value of p_{tissue} for which all the weights are positive! These results indicate that the traditional optimization yields poorer results as the overlap between beams becomes larger in the region outside the PTV.

4.3 Results using FIDO

In this case we optimized the FIDO objective function

$$O_{FIDO} = p_{PTV} O_{PTV} + p_{tissue} O_{tissue},$$

with the *PTV* and *tissue* terms defined respectively in equations (2a) and (4). No *symmetry* term, of the type of equations (5), was included for this calculation. As shown in Figures 3 and 5, when the FIDO method is used, once p_{tissue} acquires a minimally significant value ($p_{tissue} / p_{PTV} = 0.01$) for the tissue term to become relevant in the objective function (*i.e.* when FIDO "kicks in"), all the beams have the same optimized weight within the precision of the calculation. No difference is found in the case of a PTV with a larger radius.

These results are very important because they show that FIDO is not only much faster and accurate than traditional optimizations but also that there are limiting test cases in which FIDO yields correct results while *the conventional objective function (i.e. the standard optimization currently in use) provides erroneous solutions.*

5. Optimization Results

Below we present several sets of preliminary results in two dimensions (2D) obtained for a head and neck case, a prostate case and an "interlocking rectangles" phantom. In each case, we include calculation and optimization times for primary KERMA calculations as they were obtained on a single-processor desktop PC. The program was written in C# using the Microsoft .NET environment. No effort has been devoted to maximize the speed of the matrix inversion procedure.

In all cases the number of gantry angles used is evenly distributed over a full 360 degree circle around the isocentre. In turn, each beam is evenly divided into beamlets of the specified width resulting in the total number of beamlets quoted. The source to axis distance (SAD) is 100 cm. In each case we also present the cumulative dose-volume histogram (DVH), as well as a set of iso-KERMA contours.

5.1 Head and neck case

In Figures 6 and 7 we present the isodose curves and the dose-volume histogram (DVH) for a neck tumour partially wrapped around the spinal cord with a linear dimension of approximately 11 cm. The target was irradiated with 60 equally spaced beams divided into beamlets 2 mm wide, yielding a total of 2968 beamlets. The FIDO optimization of the 2968 independent weights using a Matlab matrix inversion routine takes 5.13 seconds on a single processor desktop PC. The resulting dose distribution within the PTV is homogeneous within +/- 2% while 95% of the OAR receives a dose that is less than 5% the dose in the PTV.

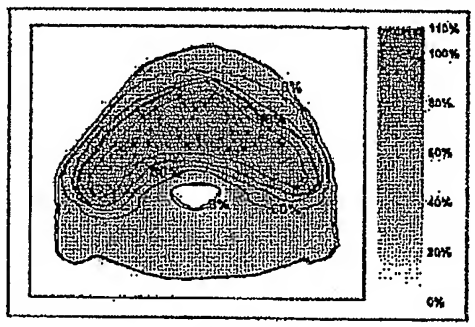

Figure 6

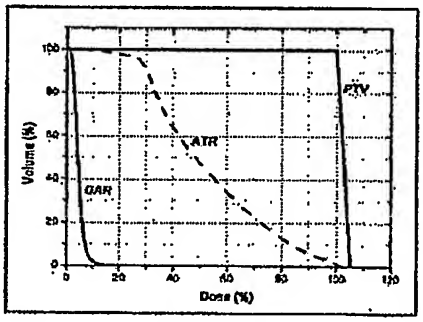

Figure 7

5.2 Interlocked square phantom case

In Figures 8 and 9 we present the isodose curves and the dose-volume histogram (DVH)

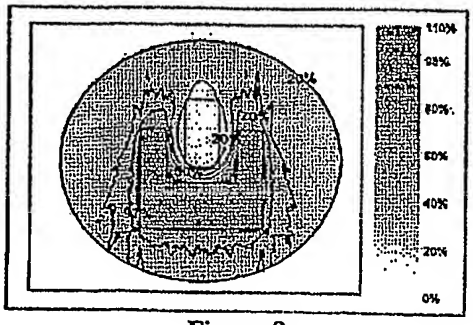

Figure 8

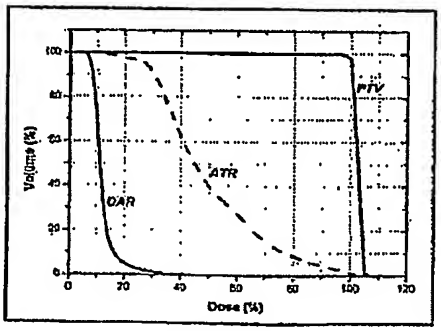

Figure 9

for a challenging "interlock" phantom. The PTV, with a linear dimension of approximately 25 cm is wrapped around half of a rectangular OAR. The target was irradiated with 40 equally spaced beams divided into beamlets 3.75 mm wide, yielding a total of 2326 beamlets. The FIDO optimization of the 2326 independent weights using a Matlab matrix inversion routine takes 2.53 seconds on a single processor desktop PC. The resulting dose distribution within the PTV is homogeneous within +/-3% while 95% of the OAR receives a dose that is less than 20% the dose in the PTV. Notice that the 97% isodose is very highly conformal and that any iso-Kerma for values greater or equal to 103% is not observed; notice as well the sharp gradient in the region between the PTV and the OAR.

In both cases above, i.e. the optimization of 2,968 beamlets and 2,326 beamlets, a Matlab minimization search routine with gradient input, using the standard objective function and constrained to positive weights, running under identical conditions as in the cases above, could not find a global minimum in less than 4 hours (at that time the program was shut down).

5.3 Prostate with overlapping rectum case

In Figures 10, 11 and 12 we present the isodose curves and the dose-volume histogram (DVH) for a prostate PTV that overlaps the rectum. The PTV, with a linear dimension of approximately 7 cm is wrapped around half of a rectangular OAR. The target was irradiated with 60 equally spaced beams divided into beamlets 4 mm wide, yielding a total of 1002 beamlets. The FIDO optimization of the 1002 independent weights using a Matlab matrix inversion routine takes 0.24 seconds on a single processor desktop PC. In Figure 10 we present a panoramic view of the slice including the femoral heads. In Figure 11, we present a close up view of the PTV-rectum region, and in Figure 12 we present the Dose-Volume Histogram – notice that in the case of the OAR we plot the DVH for the portion of the OAR outside the DVH (*i.e.* the portion that needs to be shielded). The resulting dose distribution within the PTV is homogeneous within +4% and -3% with the white dots in side the PTV in Figure 11 corresponding to 103% isodoses. Notice again the sharp conformality to the PTV of the 97% iso-KERMA as well as the sharp gradient as one enters the OAR portion outside the PTV.

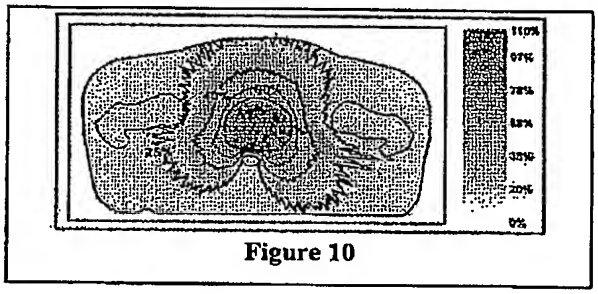

Figure 10

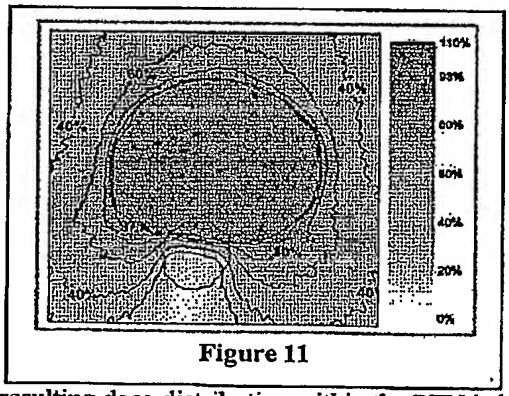

Figure 11

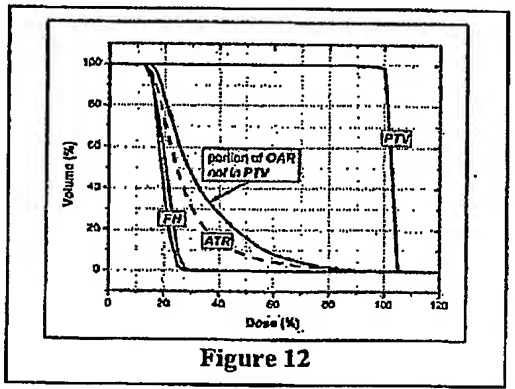

Figure 12

In this case, i.e. the optimization of 1,002 beamlets, a Matlab minimization search routine with gradient input, using the standard objective function and constrained to positive weights, running under identical conditions as in the cases above, took 3 hours and 27 minutes to converge to the global minimum.

The results above display the power of FIDO to perform optimizations extremely quickly and to provide very conformal dose distributions - both important towards the goal of adaptive radiotherapy.

6. Conclusions and future work

We have developed a fast and robust technique to find a global minimum that yields excellent results for the inverse optimization problem for the radiation treatment of tumours with IMRT, using large sets of non-negative intensity-modulated beamlets.

Work is currently in progress on a full implementation FIDO in our treatment planning system that uses collapsed cone convolution method for dose calculation (Ahnesjo 1989). Work is proceeding as well on an interactive 3D implementation that will permit "dose-adaptive radiotherapy" using CT images (Mackie *et al* 1999, Jaffray *et al*, 2002). The dose distribution can thus be reconstructed for each treatment fraction to converge to the planned optimization goals.

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FIGURE CAPTIONS

Figure 1. Concentric circular contours for the circularly symmetric case.

Figure 2. Standard optimization results for the weight ratio w_{min}/w_{max} as a function of importance parameters for a circular PTV with a 4 cm radius.

Figure 3. FIDO results for the weight ratio w_{min}/w_{max} as a function of importance parameters for a circular PTV with a 4 cm radius.

Figure 4. Standard optimization results for the weight ratio w_{min}/w_{max} as a function of importance parameters for a circular PTV with a 10 cm radius.

Figure 5. FIDO results for the weight ratio w_{min}/w_{max} as a function of importance parameters for a circular PTV with a 10 cm radius.

Figure 6. Isodose contours for a head and neck case.

Figure 7. Dose-volume histograms (DVH) for the head and neck case of Figure 6.

Figure 8. Isodose contours for an interlocked phantom.

Figure 9. Dose-volume histograms (DVH) for the interlocked phantom of Figure 6.

Figure 10. Isodose contours for a prostate case – panoramic view.

Figure 11. Isodose contours for a prostate case – close-up view.

Figure 12. Dose-volume histograms (DVH) for the prostate case of Figures 10 and 11.